

14. (amended) The adenovirus vector of claim 1, wherein said adenovirus gene essential for replication is operably linked to a composite regulatory element comprising said HRE and a tumor cell-specific transcriptional regulatory element (TRE).

15. (amended) The adenovirus vector of claim 14, wherein said tumor cell-specific TRE comprises a promoter.

16. (amended) The adenovirus vector of claim 14, wherein said tumor cell-specific TRE comprises an enhancer.

21. (amended) The adenovirus vector of claim 14, wherein said tumor cell-specific TRE comprises a prostate specific promoter and enhancer.

24. (reiterated) A composition comprising:
a replication-competent adenovirus vector comprising a hypoxia responsive element (HRE) operably linked to an adenovirus gene essential for replication selected from the group consisting of E1A, E1B and E4, wherein said HRE comprises a binding site for hypoxia inducible factor-1; and
a pharmaceutically acceptable excipient.

25. (reiterated) An isolated host cell comprising the adenovirus vector of claim 1.

26. (reiterated) A method of propagating adenovirus *in vitro*, the method comprising:
introducing into a cell an adenovirus vector comprising a hypoxia responsive element (HRE) operably linked to an adenovirus gene essential for replication selected from the group consisting of E1A, E1B and E4, wherein said HRE comprises a binding site for hypoxia inducible factor-1 wherein said cell is maintained under hypoxic conditions *in vitro*, thereby expressing said adenovirus gene essential for replication;
wherein said adenovirus is propagated.

32. (reiterated) The method of Claim 26, wherein said propagating of said adenovirus is cytotoxic to said cell.

33. (reiterated) The method of Claim 32, wherein said cell is a tumor cell.

34. (amended) The adenovirus vector of claim 14, wherein said tumor cell-specific transcriptional regulatory element (TRE) is selected from the group consisting of a prostate-specific TRE (PSA-TRE), a glandular kallikrein-1 TRE (*hKLK2*-TRE), a probasin TRE (*PB*-TRE), an α -fetoprotein TRE (AFP TRE) and a carcinoembryonic antigen TRE (CEA TRE).

35. (reiterated) A replication-competent adenovirus vector for selective cytolysis of a target cell, comprising:
an E2F-1 transcriptional regulatory element (TRE) operably linked to an adenovirus gene essential for replication selected from the group consisting of E1A, E1B and E4.

36. (reiterated) The adenovirus vector of claim 35, wherein the E2F-1 TRE is human.

37. (reiterated) The adenovirus vector of Claim 36, wherein said E2F-1 TRE comprises the nucleotide sequence set forth in SEQ ID NO:2.

38. (reiterated) The adenovirus vector of Claim 35, wherein said E2F-1 TRE comprises a nucleotide sequence having at least 80% sequence identity with the sequence set forth in SEQ ID NO:2.

39. (reiterated) The adenovirus vector of Claim 35, wherein said E2F-1 TRE comprises a nucleotide sequence that hybridizes under stringent conditions with the sequence set forth in SEQ ID NO:2.

40. (amended) The adenovirus vector of Claim 35, wherein said adenovirus gene essential for replication is operably linked to a composite regulatory element comprising said E2F-1 TRE and a tumor cell-specific transcriptional regulatory element (TRE).

41. (amended) The adenovirus vector of claim 40, wherein said tumor cell-specific transcriptional regulatory element (TRE) is selected from the group consisting of a prostate-specific TRE (PSA-TRE), a glandular kallikrein-1 TRE (*hKLK2*-TRE), a probasin TRE (*PB*-TRE), an α -fetoprotein TRE (AFP TRE) and a carcinoembryonic antigen TRE (CEA TRE).

42. (reiterated) A composition comprising:
a replication competent adenovirus vector for selective cytolysis of a target cell, comprising an E2F-1 transcriptional regulatory element (TRE) operably linked to an adenovirus gene essential for replication selected from the group consisting of E1A, E1B and E4; and
a pharmaceutically acceptable excipient.

43. (reiterated) An isolated host cell comprising the adenovirus vector of Claim 35.

44. (reiterated) A method of propagating adenovirus *in vitro*, the method comprising:
a replication competent adenovirus vector for selective cytolysis of a target cell, comprising an E2F-1 transcriptional regulatory element (TRE) operably linked to an adenovirus gene essential for replication selected from the group consisting of E1A, E1B and E4 wherein said cell is maintained under cell cycling conditions *in vitro*, thereby expressing said adenovirus gene essential for replication;
wherein said adenovirus is propagated.

45. (reiterated) The method of Claim 44, wherein said propagating of said adenovirus is cytotoxic to said cell.

46. (reiterated) The method of Claim 44, wherein said cell is a tumor cell.

REMARKS

In view of the above amendments and the following remarks, the Examiner is respectfully requested to withdraw the rejections, and allow claims 1, 8, 14-16, 21, 24-26 and 32-46, the currently pending claims. Claims 14-16, 21, 34 and 41 have been amended. No new matter is added.

Support for the amending language, "tumor cell specific" may be found in the specification on page 18, line 25.

A substitute sequence listing is submitted herewith, which has deleted SEQ ID NO:1 and renumbered the remaining sequences. No new matter is added. Entry of the sequence listing is requested. The specification has been amended to delete reference to Figure 2, and to renumber the remaining figures, in accordance with the Examiner's suggestion.